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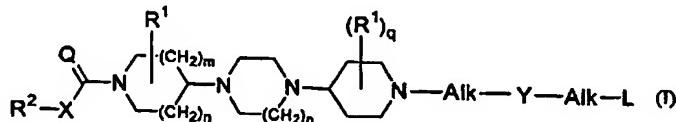
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(54) Title: SUBSTITUTED 1, 4-DI-PIPERIDIN-4-YL-PIPERAZINE DERIVATIVE COMBINED WITH AN OPIOID ANALGESIC AND THEIR USE FOR THE TREATMENT OF PAIN AND SIDE-EFFECTS ASSOCIATED WITH OPIOID-BASED TREATMENTS



and/or treatment of emesis, pain and/or nociception, in particular in opioidbased acute and chronic pain treatments, more in particular in inflammatory, postoperative, emergency room (ER), breakthrough, neuropathic and cancer pain treatments and the use of an NK₁-receptor antagonist for the manufacture of a medicament for the prevention and/or treatment of respiratory depression in opioid-based treatments of pain. The pharmaceutical formulations according to the invention comprise a pharmaceutically acceptable carrier and, as active ingredients, a therapeutically effective amount of an opioid analgesic and NK₁ -antagonists according to the general Formula (I) the pharmaceutically acceptable acid or base addition salts thereof, the stereochemically isomeric forms thereof, the *N*-oxide form thereof and prodrugs thereof, wherein all substituents are defined as in Claim 1. The pharmaceutical composition according to the invention reduces to a large extent a number of unwanted sideeffects associated with opioid analgesics, in particular emesis, respiratory depression and tolerance, thereby increasing the total tolerability of said opioids in pain treatment.

(57) Abstract: This invention concerns novel formulations for opioid-based treatments of pain and/or nociception comprising opioid analgesics and 1,4-di-piperidin-4-yl-piperazine derivatives having neurokinin antagonistic activity, in particular NK₁ antagonistic activity, the use of said formulation for the manufacture of a medicament for the prevention



TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

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